

## TREATMENT OF NON-GONOCOCCAL URETHRITIS WITH NOVOBIOCIN\*

BY

R. R. WILLCOX

*St. Mary's Hospital, London*

Novobiocin is a new antibiotic with promising antimicrobial and antiparasitic potentiality which is currently under trial in a variety of conditions. It has already been given many names by contributors to *Antibiotic Medicine* (April, 1956). It was isolated from *Streptomyces niveus* by the Upjohn Company (Streptonivacin; Albamycin) and also from *Streptomyces spheroides* by the Merck Company (Cathomycin; Cathocin). It has also been shown that Cardelmycin, manufactured by the Pfizer Company, is the same substance (Welch and Wright, 1955).

The wide antibacterial spectrum of the antibiotic suggested that it might be of use in the treatment of non-gonococcal urethritis (NGU), the aetiology of which is obscure, and a total of 42 previously untreated cases of NGU have therefore been treated with Novobiocin. Two of the patients who failed to respond were found to have gonococci in the smears a week later and have been excluded. The present report concerns the remaining forty cases.

### The Patients

Sixteen patients were Negroes, fourteen from the West Indies and two from West Africa, and 24 were white. Their average age was 30.1 years (extremes 17 to 61). Eleven patients were married, one was a widower, one was divorced, and 27 were single. Sixteen patients had no previous history of venereal disease. The remaining 24 had had between them no less than thirty attacks of gonorrhoea, 29 attacks of NGU, and one of syphilis. Six of the sixteen Negroes had experienced no previous venereal incident, but the remaining ten had had fifteen attacks of gonorrhoea and nine of NGU. The average number of previous attacks of venereal disease was thus 1.5 for both Negroes and whites.

The discharge had been present before treatment for from 1 to 3 days in nineteen cases, from 4 to 7 days in twelve, from 8 to 14 days in four, from 21 days in one, and for 28 days or over in four. The disease was apparently acquired from a stranger in 21 cases, from a friend in thirteen, and from marital exposure in six. The apparent incubation period was from 1 to 3 days in twelve, from 4 to 7 days in eight, from 8 to 14 days in four, from

15 to 21 days in three, for 28 days or over in four, and unknown in nine. Twenty patients noted some dysuria and twenty did not.

The Wassermann reaction and VDRL serum test were negative in all but one patient who had a negative Wassermann reaction and a positive VDRL test. The gonococcal complement-fixation test was performed on sera from 36 patients, being negative in 31 and positive in five. Trichomonads were sought by dark-field examination in the discharges of 27 patients and found in none.

### Results

Twenty patients were given 250 mg. Novobiocin orally four times a day for 6 days and twenty were given 500 mg. four times daily for the same length of time (Table I).

TABLE I  
RESULTS OF TREATING 40 CASES OF NON-GONOCOCCAL  
URETHRITIS WITH NOVOBIOCIN, BY DOSAGE

Schedule (over 6 days)	No. Treated	No. Followed-up	No. of Successes	No. of Failures	Per- centage Re-treated
6 g. 12 g.	20 20	18 18	7 9	11* 9†	61.1 50.0
Total	40	36	16	20	55.6

\* Includes a ? marital re-infection at 42 days.

† Includes one failure with pus in the prostatic smear without discharge and one ? re-infection at 33 days.

As the 12-g. schedule gave no substantially better results than the 6-g. schedule, the follow-up and results are considered together (Table II).

Before treatment all the patients had a pus-containing urethral discharge in which gonococci could not be demonstrated. After treatment the plan was to observe the patients weekly for one month, during which time two prostatic smears were to be examined, and then to observe them monthly (including prostatic examination) for 2 more months, unless re-treatment should be necessary for non-response or relapse.

No attempt was made to distinguish relapse from re-infection, although it is noted that nearly all failures resulted from non-response. Two failures at 1 to 2 months were considered as possibly due to

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TABLE II  
NOVOBIOCIN IN NON-GONOCOCCAL URETHRITIS

Length of Follow-up	No. Followed-up	No. of Failures
0	40	—
1-3 days	36	7
4-7 days	36	6
8-14 days	28	4†
15-21 days	21	1
22-28 days	15	2*
1-2 months	14	—
2-3 months	8	(2)
Over 3 months	7	—
Total	36	20

\* Both these cases were probable re-infections.

† Includes one failure with pus in the prostatic bead without discharge.

re-infection. A urethral discharge was present in all the failures except one in which pus was found in the prostatic secretion. Only four of the seventeen failures were Negroes who, with individual exceptions, are probably less critical of the presence of slight discharges.

### Side-Effects

No serious toxic effects were noted. Two patients complained of nausea; in one instance this was accompanied by vomiting which prevented the completion of the course. Two patients complained of looseness of the bowels and another, the only other patient who defaulted, had diarrhoea and colicky abdominal pains.

### Comparison with Other Antibiotics

The writer in the past has tested a number of other antibiotics using identical criteria of selection and subsequent observation in the treatment of previously untreated cases of NGU. In Table III the present results with Novobiocin are contrasted with this accumulated experience. From this it would appear that Novobiocin has no effect upon NGU.

### Summary and Conclusions

(1) Forty patients with NGU have been treated with Novobiocin. Of these, twenty received 1 g. in four daily doses for 6 days (total 6 g.) and twenty had twice this amount over the same time.

(2) Of the 36 cases followed, re-treatment was necessary in 55.6 per cent. The results were bad in both groups.

(3) In all, throughout a varying period of follow-up, there were only sixteen successes compared with twenty failures. Nearly all the failures were cases of non-response with persistence of the urethral discharge. In two cases, re-infection was considered likely and in one there was pus in the prostatic secretion without urethral discharge.

TABLE III  
RESULTS OF TREATMENT BY DIFFERENT MEANS OF 807 PREVIOUSLY UNTREATED CASES OF NON-GONOCOCCAL URETHRITIS

Drug	Usual Dose (g.)	No. Treated	No. Followed-up	No. of Failures	Percentage of Failures of those Followed
Oxytetracycline	5-6	85	82	13	15.9
Tetracycline	6	124	108	20	18.5
Chlortetracycline	5-6	115	108	20	18.5
Spiramycin	10-20	87	77	16	20.8
Erythromycin	6	101	85	23	27.1
Streptomycin	2-4*	62	58	22	37.9
Sulphonamides	20-28	55	53	21	39.6
Penicillin	1-3.6 mega units*	70	65	26	40.0
Chloramphenicol	5-6	39	37	15	40.5
Novobiocin	6-12	40	36	20	55.6
Placebo	—	29	22	15	68.2
Total		807	731	211	28.9

\* Given by injection.

(4) Although with the 6-day course no serious toxic effects were noted, two patients were unable or unwilling to complete therapy because of side-effects, one having nausea and vomiting, and the other diarrhoea and colicky abdominal pains.

(5) A comparison has been made with the results of different forms of treatment of other previously untreated cases of NGU which were selected and observed under similar conditions. The results obtained with Novobiocin were nearest to those in which only a placebo was used.

(6) It is concluded that Novobiocin is ineffective in the treatment of NGU.

(7) It has also been shown that in doses of 2-3 g., Novobiocin is ineffective in gonorrhoea (Willcox, 1956). The fact that NGU responds reasonably well to the wide-spectrum antibiotics: tetracycline, oxytetracycline, chlortetracycline, spiramycin, and erythromycin, but not to Novobiocin and only slightly to chloramphenicol, may provide a clue as to where to look for the aetiological agent of non-gonococcal urethritis.

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### REFERENCES

- Antibiot. Med.* (1956). 2, 205-289. (Ten articles by various contributors).  
Welch, H., and Wright, W. W. (1955). *Antibiot. and Chemother.*, 5, 670.  
Willcox, R. R. (1957). To be published in *Antibiot. Med.* (Brit. Ed.).